THE INCIDENCE AND ETIOLOGY OF BRONCHIOGENIC CARCINOMA

- A Review of Literature -

compiled by

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New York 1, N. Y.

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CIGARETTE CONCERN SCOUTS CANCER LINK

American Tobacco Head Says There Is No Proof Smoking Causes Disease in Lungs

'LOOSE TALK' IS ASSAILED

Hahn Notes That Experts Differ on Causes of Increases in Respiratory Ailments

Paul M. Hahn, president of the American Tobacco Company, spoke out yesterday in defense of cigarettes against the charge that they were injurious to health. He was the first major cigarette company executive to do so in recent months.

Mr. Hahn characterized as a lot of "loose talk" recently published scientific reports suggesting that there was a link between cigarette smoking and a rise in the incidence of lung cancer.

"It has not been proved that cigarettes have ever caused a single case of lung cancer, a statement by Mr. Hahn declared. The American Tobacco Company, which sold $1,065,738,454 worth of cigarettes and other tobacco products last year, is convinced that there is no connection between tobacco and lung cancer, he said.

Mr. Hahn also took the occasion to observe that within the last 350 years at one time or another virtually every known disease of the human body had been ascribed to the use of tobacco. One by one these charges have been abandoned for lack of evidence.

Breaks Industry's Silence

Mr. Hahn's statement broke a spell of silence that had seized cigarette company spokesmen recently. For five years, sporadic reports that lung cancer and smoking are related have appeared in scientific literature. These have received wide publicity. Two months ago, at the annual meeting of the American College of Surgeons, leading surgeons challenged tobacco companies to prove or disprove the suggestions that ciga-

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...Top-level reply to the surgeons' group has been made. But much cigarette advertising has reflected the industry's concern. Cigarette makers have assured users that their products are safe.

Mr. Hahn's statement said:

"Believing as we do that cigarette smoking is not injurious to health, I feel that a statement of reassurance to the public should be made. What the public wants to know about is whether it is true that smoking has been proved to contribute to the incidence of lung cancer. The fact, of course, is that it has not been so proved.

"With all respect to the sincerity of those who have been working in the field of lung cancer research, there has been much loose talk on the subject as reported in the press during recent months.

Offers 'Facts' in Case

"The public is entitled to know the facts. They can be stated briefly, unmistakably and confidently.

"1. Undoubtedly lung cancer is now more common than it was one or two decades ago; also undoubtedly cigarette smoking has increased, as have other habits and conditions of modern life. But that does not prove that cigarette smoking produces or contributes to lung cancer.

"2. Although all the research being conducted in this field, no one has ever proved that lung cancer in any human being is directly traceable to tobacco or to its products in any form.

"3. Authorities themselves differ widely. For every expert who blames tobacco for the increase in respiratory disease there are others who speak with at least equal authority who say that there is no evidence to show that tobacco is the cause.

Mr. Hahn said that many statisticians regarded the statistics about lung cancer and smoking as faulty, that the scientists who have produced cancer in laboratory animals with tobacco smoke had not used normal smoking concentrations of tobacco smoke and that many attributed lung cancer to other causes, to polluted air over cities, for instance, rather than to smoking.

Mr. Hahn said that the American Tobacco Company, which makes Lucky Strike cigarettes, was supporting scientific research in many independent institutions and that he was confident that long-range, impartial investigation and future objective research will confirm the view that neither tobacco nor its products contribute in the slightest to lung cancer.

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From: The American Tobacco Company
111 Fifth Avenue

November 26, 1953

Paul M. Hahn, President of the American Tobacco Company, took issue today with what he called "loose talk" on the subject of smoking in relation to lung cancer. Stating that the public should be reassured on the subject of smoking and health. He pointed out that no one has yet proved that lung cancer in any human being is directly traceable to tobacco or its products in any form.

Mr. Hahn's statement, the first of its kind by any American cigarette manufacturer, was made in answer to inquiries as to what the company is doing to meet the apparent concern of smokers about the effect of cigarette smoking on health.

Mr. Hahn's statement was as follows:

"Believing as we do that cigarette smoking is not injurious to health, I feel that a statement of reassurance to the public should be made.

"What the public wants to know about is whether it is true that smoking has been proved to contribute to the incidence of lung cancer. The fact, of course, is that it has not been proved.

"With all respect to the sincerity of those who have been working in the field of lung cancer research, there has been much loose talk on the subject, as reported in the press during recent months. Tobacco is enjoyed by so many millions of people that it is only natural that this kind of comment should create public controversy and therefore result in considerable publicity.

"The public is entitled to know the facts. They can be stated briefly, unmistakeably and confidently:

1. Undoubtedly, lung cancer is now more common than it was one or two decades ago. Also undoubtedly, cigarette smoking has increased, as have other habits and conditions of modern life. That does not prove that cigarette smoking produces or contributes to lung cancer.

2. With all the research being conducted in this field, no one has yet proved that lung cancer in any human being has been directly traceable to tobacco

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or its products in any form.

3. Authorities themselves differ widely. For every expert who blames tobacco for the increase in respiratory disease, there are others who speak with at least equal authority who say that there is no evidence to show that tobacco is the cause.

(a) There are scientists who are convinced that the growth of cigarette smoking and the increase of lung cancer are grounds for suspecting a link. On the other hand, there are many scientists who report that the statistics which are supposed to show a link between the rise in lung cancer and the increased use of cigarettes are faulty, unreliable and oftentimes meaningless.

(b) There are a few scientists who report that by using a high concentration of cigarette smoke — entirely different from smoke which a person draws from a cigarette — and painting it on the skins of mice, they have produced skin cancer on the mice. On the other hand, there are many more scientists of high repute who have made similar experiments and have reported no skin cancer was produced. Moreover, all scientists agree that there is no known relation between skin cancer on mice and lung cancer in humans.

(c) There are scientists who point to the possibility that numerous other causes may be responsible for the increase in lung cancer. For example, only a few weeks ago it was authoritatively reported by a group of scientists meeting in New York that polluted air over large cities may be the major cause of the increase in this disease.

"Now I realize that anyone in the tobacco business making these remarks runs the risk of being accused of being commercially minded. On this score, let me make two other observations:

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1. At one time or another within the past 350 years, practically every known

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disease of the human body has been ascribed to the use of tobacco. One by one these charges have been abandoned for lack of evidence.

2. The American Tobacco Company is working at and supporting scientific research of a fundamental nature in this field within its own laboratories and in independent institutions. It is our policy, within the limit of avoiding duplication of research, to extend our cooperation to projects where we believe the researchers are approaching the subject without prejudice and preconceived opinions on the problem to be investigated. All this represents an intelligent, objective approach to a subject which is susceptible otherwise to more or less sensational exploitation. We are confident that long-range, impartial investigation and other objective research will confirm the view that neither tobacco nor its products contribute to the incidence of lung cancer. We wish the public to know these facts so that they themselves may be informed and will be in a position to deal with the subject when misinformation comes to their attention."

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Time's readers and millions of tobacco smokers deserve better of you than your dangerously superficial discussion of the relationship of tobacco smoking to cancer (Time, Nov. 30).

In its release of November 27 the Damon Runyon Fund, now spending $1,400,000 annually to discover the truth about cancer, does a better job: "It is recognized that lung cancer is now more common than it was one or two decades ago. Many suggestions as to the cause of this increase have been made; the possible relationship of air pollution, vehicle exhaust fumes, smoking and other factors have been widely mentioned. Some of these surmises are purely speculative, some are drawn from statistics, others derive from the experimental induction of cancer in animals of these materials. However, none of these factors has as yet induced in experimental animals lung cancer of the kind seen in man. None of this evidence is conclusive but does urge the need for carefully controlled research to secure the answer. Three questions arise which require solution: first, is there a causal relationship; second, if so, what factors are responsible; third, how can they be eliminated?"

That none of these questions has as yet been satisfactorily answered so far as tobacco is concerned is attested by the recent statement of Dr. W. C. Hueper of the National Cancer Institute: that "It may be concluded that the existing evidence neither proves nor strongly indicates that tobacco smoking and especially cigarette smoking, represent a major or even predominating causal factor in the production of cancers of the respiratory tract and are the main reason for the phenomenal increase of pulmonary tumors during recent decades. If excessive smoking actually plays a role in the production of lung cancer, it seems to be a minor one if judged from the evidence on hand."

There is no present justification for the public alarm which you obviously seek to engender. Until the facts are fully known, you would do well to observe your own "moral obligation" to report objectively the whole truth.

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FROM: DAMON RUNYON FUND
HOTEL ASTOR
BROADWAY & 44th STREET
New York 36, N.Y.

FOR IMMEDIATE RELEASE: November 27, 1953

RUNYON FUND STUDIES AIR POLLUTION

Smog Highlights Lung Cancer Problem

The Damon Runyon Fund since its inception has been devoted entirely to cancer research. Through qualified research centers it makes available $1,250,000 a year which goes to the support of research into the cause and control of cancer. It should be noted that the Damon Runyon Fund has no overhead expenses and that all the money it receives goes out for the purpose for which it was intended. The Runyon Fund funds are allocated upon due scrutiny and review of the projects which are submitted to them by a Scientific Advisory Committee consisting of nine persons of national reputation in the cancer field.

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It is recognized that lung cancer is now more common than it was one or two decades ago. Many suggestions as to the cause of this increase have been made; the possible relationship of air pollution, vehicle exhaust fumes, smoking and other factors have been widely mentioned. Some of these surmises are purely speculative, some are drawn from statistics, others derive from the experimental induction of cancer in animals of these materials. However, none of these factors has as yet induced in experimental animals lung cancer of the kind seen in man. None of this evidence is conclusive but does urge the need for carefully controlled research to secure the answer. Three questions arise which require solution: first, is there a causal relationship: second, if so, what factors are responsible; third, how can they be eliminated?

The Damon Runyon Fund, realizing the importance of these questions and the necessity for securing both unbiased study and the efficient utilization of the scientific resources of the country, has established a plan to meet these ends. This plan provides for the Fund to serve as a clearing house for research on the problem, receiving the financial support of the industries concerned and through its Scientific Advisory Committee allocating funds into useful lines of study in qualified research centers. The tobacco industry, recognizing the fundamentally sound approach taken by the Damon Runyon Fund, has made generous financial contributions to the Fund for the support of cancer research.

In sponsoring this type of research the Damon Runyon Fund is rendering an important public service consistent with the highest standards of scientific integrity and can give assurance that every effort is being made to further our understanding of the various causes and control of cancer.

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PREFACE

The following review has been compiled after an extended search of the literature ~~and is believed comprehensive in scope~~. Most of the papers cited have been consulted in the original, and in those cases where only abstracts or citations by other workers have been inspected, this fact has been recorded in the appended Bibliography.

It will be noted that contrary to the practice followed in most surveys of literature intended for general publication, in the present review no attempt has been made to compress as much detail into each sentence and paragraph as possible. Publications alleging a carcinogenic action for tobacco or its combustion products in the animal or in the human ~~bronchiogenic carcinoma~~ have usually been treated at sufficient length that salient experimental, statistical, and clinical details are retained.

References to the literature are cited in the text by authors and year of publication, and in the Bibliography are arranged alphabetically by author. Many of the more important articles and works cited in this review are available in photostatic form in the Technical Information Files, Research Department, Philip Morris and Co., Ltd., Inc., and where this is the case the respective file numbers are given in the citation in the Bibliography.

As the interpretations of the findings of other authors and the conclusions arrived at in the present review are those of the compiler, and as the review and Bibliography are novel and original, the use of this work in the preparation of reviews or articles intended for general publication is forbidden without the express permission of Philip Morris and Co., Ltd., Inc.

The compiler wishes to acknowledge the help rendered by Miss Maria E. Michal and by Mr. Theodore Dunne in checking references, in aiding in the location of relevant articles, and in proofreading the manuscript. The author is grateful to Frank Panzarella, Ph.D. and [illegible] for helpful discussions.

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INTRODUCTION

Indent ¶ → Primary carcinoma of the lung - a clinical and pathologic rarity at the turn of the century - is now the reported cause of death in about 15,000 persons yearly in the United States.

Indent ¶ → To examine the literature bearing on the nature and magnitude of this increased death rate due to lung cancer is one objective of this review. To survey the literature bearing on the existence of special occupational, environmental or behavioral factors in the genesis of lung cancer, is a further objective.

Indent ¶ → The reader is forewarned that many aspects of our present knowledge of the etiology of lung cancer are not only clouded with controversy and with the need for more adequate and better controlled studies, but also with the unsolved mysteries of the nature of the general cancer process.

Indent ¶ → On many a page of this review the studies discussed, often in consecutive paragraphs, will be found to reach opposite conclusions. In such situations the present reviewer has acted usually only as a reporter. Resolution of most of these contrary views by rationalization has not been attempted. Usually the very existence of controversy speaks as clearly for the need for further work as any possible comments by the reviewer.

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CHAPTER I

HUMAN INCIDENCE OF LUNG CANCER

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LUNG CANCER IN THE NINETEENTH CENTURY:

Almost to the end of the nineteenth century the histogenesis and mode of spreading of tumors were only understood vaguely. Pathologists were influenced by Virchow's view that organs which are frequently the seat of metastatic involvement by malignant tumors are rarely the seat of primary growth. Many pathologists maintained that in the presence of a tumor anywhere in the body, whenever neoplastic growth was also found in the lungs, the latter growth was secondary (see Fried, 1948). It should be noted that the major advances on which histological study and differential diagnosis of bronchiogenic carcinoma depend did not occur until the 1880's or later. The advances according to Fried (1948) include:

1. Lister's antiseptic technique revolutionizing surgery and advancing the study of visceral malignant disease

2. Koch's discovery of the tubercule bacillus revealing that all cough, hemoptysis and wasting are not due to tuberculosis

3. Metchnikoff's statements (1884) on mesenchymal reactions leading to a discrimination between inflammatory and neoplastic processes.

4. Roentgen's discovery of X-rays (1896) leading to their introduction as a diagnostic aid at the turn of the century.

5. Brochoscopy and the use of iodized oil (of recent origin).

6. Surgical exploration of obscure intrathoracic conditions is still infrequent as contrasted with its use in other visceral conditions.

Discussions of the pathology and histology of lung cancer appeared in the literature soon after the discoveries of Koch and Metchnikoff, and extensive clinical reports only appeared following the introduction of X-rays. Passler in 1896 located only 96 cases of primary pulmonary cancers in the literature. Adler in 1912 found 370 cases and stated, "The failure of recognition of cancer of the lung has for a long time perpetuated the dogma of its rarity".

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THE ISSUE OF LUNG CANCER INCIDENCE:

It is clear that the incidence with which primary bronchiogenic carcinoma is observed clinically or at autopsy has increased progressively. The points at issue are what significance can be assigned when the reported incidence is extrapolated to the general population, and whether this increase in the incidence of lung cancer is real and absolute or only relative and apparent. Before attempting discussion of these issues, attention must be directed to the limitations of the very methods by which "increase" in a disease is measured, and also to the details of some of the many statistical studies of the incidence of lung cancer that have appeared in the literature.

THE RELIABILITY OF CANCER STATISTICS:

The data reported by early workers must be regarded as being of limited value because of the large errors inherent in the clinical diagnosis of lung cancer. For example Lubarsch in 1924 (according to Fried, 1948) after analyzing cancer statistics of Germany for the period 1920-1921 concluded that the errors in diagnosis in the clinical material were so great (32.4 percent) that cancer statistics of that period pertaining to the incidence and localization of tumors can have little value. In the following table the percentage of lung cancers correctly diagnosed clinically in various autopsy series has been recorded.

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TABLE

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Wells (1923, 1927) reported that in a total of 578 cases of cancer at the Cook County Hospital in Chicago, there were 211 incorrect diagnoses (32.5 percent). Wells stated, "Such a high ratio of incorrect diagnoses in a great hospital might seem to be evidence of something wrong with the hospital, but we find that other institutions dealing with a similar class of cases, of in which most of the cancer coming to necropsy are/internal organs exhibit not dissimilar figures".

Peters (1932) found that at the Moabit Hospital of Berlin during the period 1905-1909, only 3.5 percent of lung tumors were correctly diagnosed clinically, while in the period 1927-1931 this figure rose to 44.2 percent. Peters (1932) in a series at the Pathological Institute of the Berlin City Hospital reported that in lung cancers autopsied before 1913, 40-44 percent were diagnosed correctly on clinical examination, but this percentage fell to 20 percent during the period 1917-1921. Peters pointed out that when a lung neoplasm is small, it may be overlooked and only certain symptoms and complications may be recognized, and the case, therefore, misdiagnosed. Peters reported that at the Moabit Hospital in the period 1909-1912, 14.3 percent of the cases identified at autopsy as lung cancer had been clinically diagnosed as tuberculosis; in contrast this figure had fallen to 5.2 percent in 1927-1931.

Willis (1941) found the diagnosis to have been "erroneous or indefinite" in 15 out of 27 cases of cancer of the lung coming to autopsy at the Alfred Hospital, Melbourne. In a larger series of 84 autopsies performed by Willis (unpublished observations cited by Kennaway and Kennaway, 1947) on cases of pulmonary carcinoma dying in a large teaching hospital, where there was a special clinic dealing with lung surgery cases, and where full X-ray and bronchoscopic investigation was practised,

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Becker (1950) studied the records of the Surgical Clinic of the University of Giessen, Germany for the period 1928-1948. The clinical diagnosis did not correspond to the autopsy findings in 71 of 148 cases of bronchial carcinomas (49.2 percent). In 17 further cases (11.3 percent) only suspicion of a lung tumor had been recorded without clinical confirmation. In 51 percent of the 71 misdiagnosed cases a metastatic growth had been mistaken for the primary growth.

Other studies bearing on the degree of reliability of statistics on the clinical incidence of lung cancer are discussed in a later section of the chapter entitled "The Effects of Improved Diagnosis on Lung Cancer Incidence".

It must be admitted that the diagnosis of primary bronchiogenic carcinoma still appears to be difficult to establish, even under the most favorable clinical conditions.

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METHODS OF MEASURING "INCREASE" IN THE INCIDENCE OF A DISEASE:

Generally speaking, there are two yardsticks by which "increase" in the incidence of a disease may be measured. Macklin (1942) has called one the incidence yardstick by which is determined either the morbidity rate or the mortality rate of a disease. In the case of measles, these two rates would differ markedly, but in the case of lung cancer the two would correspond closely (that is, few cases of measles die of that disease, while most lung cancer cases do die of cancer). The second has been called the ratio yardstick by which is measured the ratio between death due to the disease in question and the total number of deaths. A disease may be increasing according to both yardsticks; it may be decreasing by both; it may be increasing by one and decreasing by the other; or it may be remaining stationary by one or both of the measures. The "incidence yardstick" may be measured by the number of deaths from the disease per unit population (deaths per 100,000 population is a common example) and unless a small specified age and sex group is being considered, the death rate (or the morbidity rate) may be as much influenced by birth rate as by the number of those dying from the disease. The"ratio yardstick" is as much influenced by the behavior of other diseases as by the behavior of the disease being studied (Macklin, 1942).

Macklin (1942, 1948) discussed the pitfalls existing in the interpretation of statistical data on lung cancer. He emphasized the importance of the unrecognized case. There remains in every disease and particularly in diseases like lung cancer in which the identification tag is not displayed externally (as in scarlet fever, lip cancer, etc.) an unidentified residue which may be numerically large. With lung cancer, incidence and ratio studies based on autospy findings are open to question as only a negligible portion of the population comes to autopsy.

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Macklin (1942) considered critically the application of the yardsticks discussed above in determining "increase" in the incidence of lung cancer, and the discussion of that worker is considered in the following paragraphs.

The methods that have been most commonly employed in studies of lung cancer incidence, include:

1. The ratio of lung cancer autopsies to total autopsies.
2. The ratio of lung cancer autopsies to all cancer autopsies.
3. Comparison of hospital admission rates based on clinical diagnoses.

Method (1) is considered to be inadequate by Macklin (1942) on several grounds. First, dissimilarity of age in the two autopsy groups may exist. Further, only a small fraction of the total population in a community come to autopsy and the true picture of the population affected with lung cancer may not be shown by this method. A third fallacy is one which has to do with the physician's desire to verify a diagnosis or to find a cause of death when clinical diagnosis has been impossible. In early years of this century lung cancer cases were sometimes misdiagnosed as tuberculosis and hence they were less likely to be subjected to autopsy. A further fallacy exists in the possibility, indeed probability, of changes in the autopsy population, that is, few infectious diseases come to autopsy, for example.

Method (2), the ratio of lung cancer autopsies to all cancer autopsies, suffers according to Macklin (1942) from most of the objections raised

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against method (1) above. It is to be granted that the autopsy population is more apt to be uniform than with method (1), but still the proportion in which cancers come to autopsy may be far from representative of the proportions in which they occur in the general population. A related objection is that the type of cancer coming to autopsy may have changed during the period. For example, today the physician may not be as eager to verify a diagnosis of breast cancer or lip cancer by autopsy, but may be more interested than formerly in clarifying the symptoms of lung cancer in obscure cases. Improved clinical diagnosis and therapy in other cancers has also affected the number of such cancers coming to autopsy, and may therefore produce an apparent rise in lung cancer autopsies. Also paralleling the last objection, the effect of better diagnosis of lung cancer alone would have a great effect on lung cancer increase; especially since the obvious symptoms of lung cancer are few as compared to those of external cancers of the lip, breast, etc. or even of those of rectal or uterine cancer. Finally, alterations in the sex ratio in autopsy cases during the period of statistical study, unless corrected may affect results seriously

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Method (3), the use of hospital records as basis of comparison, has been employed in some studies, as some of the above fallacies have been recognized in the use of autopsy records alone. ~~Often the basis of study is made~~ The ratio of lung cancer cases ~~admitted~~ to total hospital admissions is often made the basis of study. Many of the criticisms applying to methods (1) and (2) hold here according to Macklin (1942). In addition, the nature of cases admitted to a given hospital may differ markedly from time to time. Addition of a new ward, wing or service may affect the number of certain disease cases accepted, and the introduction in recent years of specific therapy for many infectious diseases has reduced their severity and freed beds for other cases.

([redacted], 1942).

In summary, some of the conclusions of Macklin (1942) are worth quoting at length:

"... The question we wish to determine is not whether lung cancer, meaning by that diagnosed lung cancer, is increasing in hospital cases, but is diagnosed lung cancer increasing in the population of the age and sex distribution which is capable of showing it? Therefore, the only way of determining this point is to study the incidence of diagnosed lung cancer in the population at large, and not in the small fragment of the population which comes to autopsy. Therefore, data from all hospitals within a state for two periods chosen so that the age and sex distribution of the population of the state is known, thus preferably in a census year, should be added together and analyzed. States are not large enough in their scope, since they draw disease cases from surrounding rural areas in different proportions in various years. Each state, however, has usually centers that are apt to draw patients from within their own borders.

"... It will probably be found that diagnosed lung cancer is increasing both relatively and absolutely, but the increase will probably be much smaller than is marked than by the rates adopted by most workers, in which a [redacted] distribution of [redacted] lung cancer cases and of the standard [redacted] will be [redacted]

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being diagnosed in more cases in which it exists than was formerly the case, and will be increasing no doubt because persons of lung cancer age are having fewer diseases to die of today than they had before, and hence must die in ever increasing numbers of the ones which remain.

"6. The data which are used to support the idea that lung cancer has increased faster than other forms of cancer cannot be used to support that conclusion, since we do not know what proportion of lung cancer cases were unrecognized formerly and what proportion are unidentified today. We can merely state that diagnosed lung cancer is increasing at a rate which appears to be faster than that of other diagnosed cancers.

"7. The search for environmental factors supposed to be the basis of the unduly great increase in lung cancer should await further proof that the increase in diagnosed cases has been as spectacular as it has been claimed to be."

It is in the light of the above expressed critical attitude that the ~~the~~ clinical and autopsy incidence of lung cancer reported in the following literature and summarized in the following pages should be approached.

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Aware of the need for suitable methods of demonstrating the evolutional tendency of lung cancer incidence, Fruhling and Horrenberger (1952) speculated as follows: The simplest method would be to use the data furnished by death certificates. However, too many diagnoses are either erroneous inaccurate or absent and even intentionally falsified, which would render the statistical data invalid. The use of clinical diagnostic data on lung cancer of a hospitalized group from a service that is specialized or not, introduces two more factors: One is due to variation in hospital groups from the medico-social point of view and the other is influenced by diagnostic progress. Similarly, data collected from a center for histoligical examination of biopsy samples are open to question because of the increased use of bronchoscopy. Finally, there is the possibility of using statistical data taken from autopsies. There the cause of error would be negligible as long as they have bearing on a population of sufficient numerical importance, and would serve in the study of incidence and variation in incidence of a given disease, in so far as it is a mortality cause.

Reviewing the studies that have been made in various countries, Fruhling and Horrenberger find it remarkable how different and

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often contradictory ~~their~~ results are. This, however, does not mean that the methods used are wrong, but on the contrary they seem to lend authenticity to the differences, geographic and others, in the evolutional tendency of the incidence of lung cancer." Most striking, for example, is the fact that pulmonary cancer is still rare in Iceland (Dungal 1950) while in the continental countries its incidence is 10 to 20 times greater within a corresponding period. Therefore, they feel that the various data should be considered strictly valid for the particular region from whence they come, for the material studied, and for the period within which the autopsies were made. Generalization of results should not be attempted except with extreme caution.

The studies considered in the following sections of this chapter on the incidence of lung cancer as determined from clinical and autopsy material should be approached with the realization that the methods employed to measure "increase" are subject to the severe criticisms expressed above.

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[redacted] STUDIES OF LUNG CANCER INCIDENCE ~~USE TO ABOUT 1930~~ PUBLISHED BEFORE 1934:

In this and the following sections of this chapter some of the more extensive statistical studies of the incidence of lung cancer are considered roughly in chronologically order according to the date of publication.

As stated in an earlier section the diagnosis of primary carcinoma of the lung was made only rarely by the clinician and by the pathologist until after the turn of the Twentieth century. Pässler (1896) located only 57 cases of primary pulmonary cancer in the world literature, and Adler (1912) located only 360 cases. The latter worker stated, "The failure of recognition of cancer of the lung has for a long time perpetuated the dogma of its [redacted] rarity".

Data taken from some of the early studies of the incidence of lung cancer based on autopsy statistics and covering the period up to about 1930 are given in tabular form below.

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TABLE

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The ranges of the percentages reported in the preceding table are reported in the following brief table, and do show the increase in lung cancer incidence recorded in autopsy series.

Ranges of Percentage of Lung Cancer Incidence Reported in Studies Based on Autopsy Data Covering the Period up to about 1930 (based on preceding table)

Decade	%age Lung Cancer of All Cancer		%age Lung Cancer of All Autopsies	
	Range	Simple Av.	Range	Simple Av.
up to 1890	0.92	0.9	0 -0.06	0.04
1890-1900	1.5- 4.1	2.8	0.22 - 0.44	0.33
1900-1910	1 - 4.2	2.7	0.31	0.31
1910-1920	2.0-11.1	6.5	0.42 - 0.46	0.44
1920-1930	5.6- 18.0	10.1	0.83 - 2.57	1.38

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Katz (1927) , in work cited by Matz (1938), investigated all cases of primary lung cancer in the autopsy records of the Heidelberg Pathological Institute for a sixty-year period. He concluded that the incidence of pulmonary cancers and of all cancers for the years 1906 to 1926 showed a relative as well as an absolute increase.

Brandt (1927) observed the incidence of primary lung cancer showed at first a gradual increase followed by a more rapid increase, the gradient of which became constantly steeper during the 1920's. However, the time order of these developments were different in various localities, apparently reaching its peak in Riga as early as 1916, but continuing upwards in other localities.

Simpson (1929) doubted that any improvement in clinical diagnosis of lung cancer had occured, and reported that the greatest clinical error in diagnosis was in the year 1924. After statistical study he concluded that the increased incidence of carcinoma is real and that it is not associated with a comparable increase of total carcinomas. Bonser (1929) reported an increase in the frequency with which the clinical diagnosis of primary carcinoma of the lung was made from 0.127 to 0.253 percent of all hospital admissions over a period of 41 years, while the incidence at autopsy remained relatively constant.

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The incidence of primary lung cancer at Johns Hopkins Hospital for the period 1890-1930 has been reported by MacCallum (1930). His data are given in the following table:

LUNG CANCER INCIDENCE, JOHNS HOPKINS HOSPITAL
(MacCallum, 1930)

Years	No. of Autopsies	No. of Carcinomas		% Lung Cancer of All Cancers
		All	Lung	
1890-1895	606	72	0	0
1895-1900	856	73	1	1.39
1900-1905	988	84	0	0
1905-1910	868	82	4	5.00
1910-1915	943	75	2	2.60
1915-1920	1848	95	3	3.15
1920-1925	2315	113	7	5.20
1925-1930	2830	186	13	7.00

MacCallum commented:

> "If we judge from hospital autopsy statistics, a slight but perceptible increase in the cancers of the lung has occurred. Such figures must, however, be received with great caution... Statistics must be examined very critically because so many factors may vitiate the conclusion, and in endeavoring to estimate the results of the study of 10,000 autopsies in the Johns Hopkins Hospital we have found it almost impossible to give precise weight to each of these objections."

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Rosahn (1930) totaled the data of Berblinger (1925), Breckwoldt (1926), Fuchs (1886), Hanf (1927), Holzer (1925), Katz (1927), Kikuth (1925), McCrae and co-workers (1927), Marchesani (1924), Materna (1924), Moise (1921), Pässler (1896), Reinhard (1878), Sonnenfeld (1926), Staehelin (1925), Wahl (1927), Wolf (1895), and the data of the Boston City Hospital. Rosahn's summation is presented in percentage form in the following table.

PERCENTAGE INCIDENCE OF PRIMARY LUNG CANCER
(Summation of autopsy data of 18 authors)
adapted from Rosahn, 1930

Year	Total Cancers / All Autopsies	Lung Cancer / All Autopsies	Lung Cancer / All Cancers
to 1899	8.11%	0.14%	1.45%
1900-1904	8.34	0.21	2.54
1905-1909	10.32	0.35	3.50
1910-1914	10.39	0.44	4.52
1915-1919	10.19	0.43	4.30
1920-1924	12.47	0.81	6.61
1925-1928	15.43	1.36	8.79
1910-1919	10.27	0.44	4.39
1920-1928	12.90	0.89	6.98

Rosahn concluded that the above data showed a steady rise in the relation of the number of cases of primary lung cancer autopsied to the total number of cancer cases autopsied and also to all cases autopsied. Rosahn also noted that the data showed a steady rise in the relation of the number of all cancer cases autopsied to all conditions autopsied. The total number of lung cancer cases on which the above table is based amounted to 972 cases. Rosahn excluded from the table 1,010 lung cancer cases reported during the same period either because of the incompleteness of data or because of questionable techniques of autopsy reporting. However, seventeen of these excluded authors, according to Rosahn, recognized an increase in lung cancer incidence

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

The autopsy material of the Moabit General Hospital (Berlin) was analyzed by Feilchenfeld (1901), Bejach (1917), Redlich (1917), Wahl (1927), and Peters (1932). The percentage ratio of lung cancers autopsied to all cancers autopsied underwent the following changes with time: 4.3 percent during 1895-1900, 6.3 percent during 1900-1905, 4.9 percent 1905-1908, 4.8 percent 1908-1913, 6.2 percent from 1913-1917, 6.06 percent from 1917-1922, 13.0 percent 1922-1927, 15.4 percent 1927-1931. The highest percentage was reached in 1929 with 19.2 percent with a smaller peak in 1924 of 16.5 percent. Peters (1932) treated additively the data of the Charite, Friedrichshain, Neukölln, and Moabit Hospitals in Berlin employing the data of Hanf (1927), Biberfeld (1926), Herz (1930), Kuhn (1930), Feilchenfeld (1901), Bejach (1917), Redlich (1917), Wahl, (1927), and arrived at the following percentage ratios of lung cancer at autopsy to all cancer at autopsy in the Berlin area: 4.4 percent for 1895-1900, 4.7 percent for 1900-1905, 3.5 percent for 1905-1908, 6.0 percent for 1908-1913, 4.4 percent for 1913-1917, 5.3 percent for 1917-1922, and 9.3 percent from 1922-1927. Peters emphasized that the major increase in incidence of lung cancer at autopsy occurred after 1921, but had started relatively simultaneously in various countries and increased continuously for over thirty years. Hueper (1942) commented on Peters' conclusion to the effect that this increase in many localities has not been uniform in degree or intensit

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Lemon and co-workers (1932) reported that at the Mayo Clinic since 1925 the number of primary bronchiogenic carcinomas seen had steadily increased. They reported that three times as many positive diagnoses were made in 1931 as in 1927. They concluded that there has been an actual increase in this type of tumor.

Hruby and Sweany (1933) collected 185,434 autopsies performed from 1897 to 1933. There were 22,712 cancer cases in this series, of which 1,355 were lung cancers. Cancer in general had increased 65 percent during this period, while lung cancer had increased from 4.1 percent of all cancers in 1897 to 16 percent in 1928. At first the increase in lung cancer incidence paralleled the trend for cancer generally, but since 1914 it was higher.

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STUDIES OF LUNG CANCER INCIDENCE PUBLISHED DURING 1934-1942

Bonser (1929,1934) reported no change in the incidence of primary bronchiogenic carcinoma in relation to total autopsies, total cancers, or hospital admissions at the Leeds Infirmary. A slightly higher incidence was observed during the five-year period ending in 1932, but this was only slightly in excess of the incidence for the five-year period from 1908 to 1912. In surveying the European literature, this worker reported an increase in the incidence of primary lung cancer in 32 autopsy series, only a slight increase in 5, and no increase in 8 series.

Data from some of the studies of the incidence of lung cancer based on autopsy statistics and published during the period 1934-1942 are given in tabular form below:

SOME STUDIES OF LUNG CANCER INCIDENCE BASED ON AUTOPSY DATA AND PUBLISHED DURING THE PERIOD 1934-1942

Author & Publication Date	Period Covered	%age Lung Cancer of All Cancer	%age Lung Cancer of All Autopsies	Other Data (no's of cases refer to lung cancers)
Hill, 1934	early 30's	>8	ca.1	(estimation)
Olson, 1935	1925-1929	7.68	0.11	Boston City Hosp.
" "	1930-1934	12.96	1.44	" " "
Jaffe, 1935	early 30's	11.5	-	Cook County Hosp., Chicago
Arkin & Wagner, 1936	early 30's	6.8	-	(estimation)
Rosedale & McKay, 1936	1927-1936	7.5	-	Buffalo City Hosp. (35 cases)
Simons, 1937	1899	-	0	(data of 11 N. Am.
" "	1930	-	1.55	authors for 22,754 autopsies,
" "	1910-1914	5.88	-	137 cases)
" "	1925-1928	8.28	-	
Matz, 1938	1927-1937	13.7	-	U.S. Vet. Admin. (160 cases)
Boyd, 1939	1925-1936	1.2	-	Univ. Toronto (53 cases)
" "	1927-1937	2.6	-	Winnipeg (64 cases)
Müller, 1940	1931	8.14	0.67	Cologne Path. Inst.
" "	1937	11.97	1.03	" " "

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Rosahn, 1940	1917-1927	7.35	-	(7 cases Yale Med. School
" "	1928-1937	11.04	-	(33 cases) " " "
Ochsner & DeBakey, 1941	1931	-	0.47	(3 cases) Charity Hosp.
" " "	1938	-	2.0	(17 cases) " " N. Orleans

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Olson (1935) extended the earlier data of Rosahn (1930) for Boston City Hospital, 1934, and presented the following table:

LUNG CANCER AT BOSTON CITY HOSPITAL
(Rosahn, 1930; Olson, 1935)

Years	No. of Adult Autopsies	Carcinomas		Primary Lung Cancer		
		No.	% of Autopsies	No.	% of All Autopsies	% of All Carcinomas
1900-1904	931	57	6.12	2	0.21	3.50
1905-1909	865	52	6.01	4	0.48	7.69
1910-1914	438	34	7.76	2	0.45	5.88
1915-1919	526	45	8.55	2	0.38	4.44
1920-1924	957	99	10.34	7	0.73	7.07
1925-1929	1532	182	11.87	14	0.11	7.68
1930-1934	2624	293	11.16	38	1.44	12.96
	7873	762	9.67	69	0.87	9.05

Olson concluded, "There was an abrupt increase, probably due to tremendous expansion of the Boston City Hospital in recent years; increased interest in pulmonary surgery; many patients were allowed to remain in the hospital whereas formerly they were sent to institutions for incurables."

The marked rise for the period 1930-1934 was considered by Olson to be a "selective phenomenon". It should be noted that considering the same data through 1928, Rosahn (1930) concluded: "The increase in primary carcinoma of the lung is evidently much greater than the increase in all cancers. The group is of course too small to indicate an absolute increase in lung carcinoma, but the results are highly suggestive of a real rise in incidence."

Jaffe (1935) reported that in a series of 6800 autopsies at the Cook County Hospital, Chicago, the incidence of primary carcinoma of the lung was 11.47 percent of 871 cases of carcinoma. In earlier work in Vienna, Jaffe had autopsied 4500 cases in the period 1915-1918 and reported the incidence of primary pulmonary carcinoma to be 10.73 percent of all malignancies. He concluded from his work at Vienna and Chicago that he was "inclined to believe with Fried and others that the increase in frequency of primary carcinoma of the lung is more apparent than real".

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Passey and Holmes (1935) reported combined figures of seven major hospitals in Great Britain for the period 1894-1928, inclusive. Their data ar presented in the following table:

INTRATHORACIC CANCER AT AUTOPSY AS %AGE OF ALL AUTOPSIES AND OF ALL ADMISSIONS AT CERTAIN BRITISH HOSPITALS
(Passey and Holmes, 1935)

Years	All Admissions	All Autopsies	Lung Cancers at Autopsy	%age Lung Cancer Autopsied of All Admissions	%age Lung Cancer Autopsied of All Autopsies
1894-1898	315,059	16,534	173	0.055	1.05
1899-1903	374,207	18,822	180	0.048	0.96
1904-1908	420,595	21,821	234	0.055	1.07
1909-1913	597,193	28,637	331	0.055	1.06
1914-1918	625,833	24,098	257	0.041	1.07
1919-1923	671,846	23,726	386	0.057	1.63
1924-1928	786,912	26,110	552	0.070	2.11

Passey and Holmes arrived at the conclusion that up to 1929 "....the evidence afforded does not support the widely held view that the incidence of intra-thoracic neoplasia is appreciably on the increase, especially if due allowance be made for the altered conditions of today in comparison with those of the pre-war.." (that is, before World War I). Passey and Holmes also analyzed available statistics for some of the teaching hospitals in Great Britain and concluded that up to 1929 there was no increase in the incidence of lung carcinoma in eight hospitals and only a variable increase in eight others. They suggested that the increase in these latter eight was due to special circumstances and did not represent a real increase. The data from several of these hospitals had earlier been studied in a somewhat different manner by Duguid, who had concluded that the data suggested an actual increase.

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E.L. Kennaway (1950) and Heady and Kennaway (1949) observed that some recent workers have cited the study of Passey and Holmes to support the view that we do not know whether any increase in the incidence of lung cancer has occurred . However, most of the increase in lung cancer observed by most workers has taken place since 1928, the last year of the data of Passey and Holmes. Between 1928 and 1948, the deaths attributed to lung cancer in England and Wales increased 10.4 times for men, and 5.6 times in women (814 to 8500 cases, and 314 to 1755 cases, respectively).

Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Frissel and Knox (1937) stated that "...it would seem probable that...the increase in the incidence of bronchial carcinoma in the last two decades is apparent rather than real".

Simons (1937) tabulated the data presented by eleven other North American workers and concluded that the incidence of primary lung cancer was increasing both relatively and absolutely. Simons argued that the view that the increase is only apparent can be refuted by the fact that the increase was gradual until the early 1900's, that the gradient of the increase has become constantly steeper since then, and that in various localities the greatest incidence was reached in 1924, while in others it was still increasing in 1937.

Mattick and Burke (1937) reported that at the Institute for the Study of Malignant Diseases, of 30,000 patients admitted, showing 18,000 malignant tumors, 73 (1 in every 250 malignancies) had bronchiogenic carcinoma.

Stein and Joslin (1938) expressed the opinion that the increase in primary lung cancer is due to greater diagnostic accuracy and observed that this increase was a steady one in contrast to that in the incidence of carcinoma of the larynx and the lip from 1931 to 1936.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Matz (1938) on the incidence of primary bronchiogenic carcinoma seen by the U. S. Veterans Administration from 1927 through mid-1937. Matz's study was based on autopsies performed in Veteran hospitals (such being performed in about 41 percent of all deaths). The percentage ratio of lung carcinoma to all autopsies varied from a low of 0.4 to a high of 5.3, the highest percentage being found in the first half of 1937. The percentage ratio of lung carcinoma to all carcinomas varied from a low of 2.7 to a high of 23.4, and for the entire period about 13.7 percent of all carcinomas were of the bronchiogenic type. The total number of primary lung tumors was 160, all carcinomas found amounted to 1,167, and the total number of autopsies performed was 7,398. Matz concluded that the ratio of primary lung cancer to all autopsies increased 120.8 percent from 1932 to 1937. In the same period the ratio of lung cancer to all cancer increased 69.6 percent. Matz felt that if the increased incidence of lung cancer were dependent on and due to an increase of all carcinomas, the percentage ratio each year would be about the same and would be constant over a period of years. On graphing, however, the trend was definitely upward. Matz, therefore, concluded that the increase in the incidence of bronchiogenic carcinoma was absolute. To further support this conclusion, Matz studied the incidence of cancer of the colon and prostrate from 1931 through mid-1937, and the ratio of these cancers to all carcinomas. He found little annual variation in the incidence of these cancers and in their ratio to the total number of carcinomas. Matz admitted that in addition to an absolute increase bronchiogenic carcinoma, his data showed some relative increase as well. This relative increase he held was due to expansion of the facilities for the diagnosis and treatment of cancer and also to an incfease in the age of the hospital population (average age of veterans changed from 40 to 47 years). Further, this age group 40-47 years is the one in which the largest number of lung cancers was found.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

In 1939, the Metropolitan Life Insurance Company (Anonymous, 1939) reported that cancer of the lung and pleura took a toll of about 5,000 lives a year in the United States. The death rate in 1939 from this disease was more than five times that registered twenty years previous. Among the industrial policy holders of that company, the standardized death rate from lung cancer for the age group 45-74 rose from 2.6 per 100,000 in 1917-1918 to 15.0 per 100,000 in 1937-1938. The corresponding increase in mortality for cancer of all sites during this same period was only 12 percent. It was observed that much of the increase in the incidence of lung cancer could be explained by the ~~ever~~ growing number of physicians that have become more alert to suspect this disease and have become better qualified to diagnose it, partially through the increasing use of new and improved diagnostic aids.

Müller (1939) presented autopsy data for the Cologne University Pathological Institute for the period 1930 through 1937. The incidence of lung cancer at autopsy increased from 0.67 percent of all autopsies (7 cases out of 1,039 autopsies) in 1931 to 1.03 percent (17 cases in 1,650 autopsies) in 1937 or 8.14 percent and 11.97 percent of carcinomas autopsied in these respective years. Huismann (1943) analyzed Müller's data statistically and concluded that the differences in the incidence rates observed were not statistically significant because of the small number of lung cancer cases actually autopsied and the resulting huge standard errors associated with the ~~early~~ incidence figures.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Rosahn (1940) reviewed the autopsies performed at Yale University School of Medicine from September 1917 through December 1937. A total of 435 carcinomas occurring in 425 persons were observed in 4,114 autopsies. During the period 1917-1927 there were 10 primary pulmonary tumors, or 7.35 percent of the 136 carcinomas seen, During 1928-1937, 33 pulmonary tumors were seen, or 11.04 percent of the 299 carcinomas encountered. With the exception of prostatic carcinoma, carcinoma of the lung was the only neoplasm increasing appreciably during the latter decade. Rosahn analyzed the various factors cited by earlier authors as evidence that cancer of the lung had shown only a relative increase in incidence. He attempted to meet partially the factor of improved clinical and pathological methods of diagnosis by a re-examination of the pathological slides and restudy of the clinical findings; in only two cases were the original findings altered after such review and restudy. Rosahn also discussed the view advanced by some workers that the increase in lung cancer is due to increased attention to this malady. He concluded that if this is so the "curve of attention to carcinoma of the lung would have to

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

so the curve of attention to carcinoma of the lung would have to show a positive linear trend paralleling the increased incidence of pulmonary tumors", and that "it would be necessary to assume also that in the years under discussion the attention to and interest in tumors of other organs were maintained at a constant level". According to Rosahn neither of these hypotheses is susceptible of proof.

Rosahn (1940) also reported that the general autopsy population of persons over twenty years of age shifted to a higher age level during the period from 1928 to 1937 as compared with the previous decade. He concluded that this shift, however, did not account for the observed increase in the incidence of primary pulmonary tumors.

No ¶

Rosahn considered that in his autopsy series the increase in pulmonary cancer was real and absolute. He suggested that indirect evidence would indicate that this conclusion was also applicable to the general population. He granted, however, that carcinoma of the lung is the most frequently misdiagnosed malignant tumor. In criticism of Rosahn's findings, it may be noted that his autopsy material actually only contained 43 cases of lung cancer spread over a period of 20 years and this indeed is a small number of cases on which to draw such sweeping conclusions!

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Menne and Anderson (1941) studied the occurrence of bronchiogenic carcinoma in the Pacific Northwest by sending out a questionnaire to the members of the Pacific Northwest Society of Pathologists requesting autopsy data for the period 1920-1940. Their data are presented in the following table:

INCIDENCE OF LUNG CANCER IN PACIFIC NORTHWEST
Menne and Anderson, 1941

Years	Number of Cases at Autopsy
1920-1925	3
1926-1930	63
1931-1935	201
1936-1940	407

Menne and Anderson also presented autopsy data from the University of Oregon Medical School and the Vancouver General Hospital that is given in tabular form below:

INCIDENCE OF LUNG CANCER AT UNIVERSITY OF OREGON
Menne and Anderson, 1941

Years	Cancer Autopsies	Lung Cancer Autopsies	% of All Cancers
1928-1933	3129	23	0.73
1934-1937	2820	26	0.92
1938-1940	2022	34	1.68

INCIDENCE OF LUNG CANCER AT VANCOUVER GENERAL HOSPITAL
Menne and Anderson, 1941

Years	Cancer Autopsies	Lung Cancer Autopsies	% of All Cancers
1928-1933	2111	35	1 65
1934-1937	2206	40	1 81
1938-1940	2240	[illegible]	2 [illegible]

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Menne and Anderson (1941) were impressed by the "astonishing and sharp" rise during the last two periods (1931-1935, and 1936-1940) and concluded that there had been both a relative and absolute increase of bronchiogenic carcinoma. They believe that the higher percentages observed in the Vancouver General Hospital series were probably due to less generalization in the performance of autopsies. In other words, a greater percentage of autopsies may have been performed on all patients with bronchiogenic carcinoma, because of the unusual character of their disease, than on patients with other conditions, whose death was not due to a malignant tumor. ~~These workers concluded from a detailed analysis of their statistics that there has been a relative and an absolute increase of bronchiogenic carcinoma.~~

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Husted and Biilmann (1936) at the Rigshospital in Copenhagen studied the 41 cases of lung cancer seen at autopsy from 1911 to 1934. From 1924 on, they claimed an absolute and a relative increase in the number of patients with primary lung cancer. From 1929 to 1933, pulmonary cancer was encountered in between one and two percent of all autopsies and in about 7.3 percent of all cancer cases. Eskelund (1942) extended the autopsy ~~theories~~ series of Husted and Biilmann through 1941 at which time a ~~dept.~~ department of lung surgery was established at this hospital. The number of admissions in the period 1913 - 1930 inclusive was about equal to those in the period 1931 - 1941 inclusive. The total number of hospital deaths was somewhat smaller in the earlier period, but the autopsy rate was relatively constant over the entire time. Of 70 lung cancer cases autopsied, 56 were seen after 1930, and ~~this worker~~ Eskelund concluded that this is a statistically significant increase. He pointed out that the only major change in the patient population took place in the last half of the latter period with the erection of a neurosurgical unit.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

STUDIES OF LUNG CANCER INCIDENCE PUBLISHED DURING 1943-1945:

The table appearing on the next page summarizes the data presented in various studies of lung cancer incidence based on autopsy data and published during the period 1943-1945. For convenience in tabular presentation this table includes for studies from the period 1943-1950, and hence the data should be considered not only in association with the present section of this chapter, but with later sections as well.

(Typist the table on page 40 of this draft should occupy the next full page following the above paragraph. In other words keep typing text until you fill up the page on which the above paragraph appears and then use the next page for the table, and again contuing the text on the second page.

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~~1943~~

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In 1943, Dorn of the ~~United States~~ U.S. Public Health Service, ~~reported a study of~~ studied the incidence ~~and prevalence~~ of cancer of the lung as determined from death certificates and registrations throughout the United States. According to an earlier study of Gover (1939) from the same Federal agency, between 1914 and 1930 the death rate from cancer of the lungs and pleura increased 3.7 times compared with an increase of 20 percent for all forms of cancer ~~combined~~. In the same period, the change among males exceeded that among females, the relative increases being 4.5 and 2.6 times, respectively. According to Dorn, the death rate from cancer of the lungs and pleura continued to increase from 1930 to 1940. After eliminating the effects of changes in the age composition during the latter decade, the death rate from cancer of the lungs and pleura increased 22 per cent among white females and 78 per cent among white males, or roughly about 2.5 and 8.5 percent per year, respectively. Between 1914 and 1931, the average annual increases were approximately 8.0 and 10.5 per cent, respectively, for females and males, which indicated to Dorn that the rate of increase in the death rate due to cancer of the lungs and pleura is becoming smaller.

Dorn further found that the mortality rate from other forms of respiratory cancer increased even more than the rate for lungs and pleura. In the white male population, the rate for total respiratory cancers doubled (an increase of 102 per cent) during the latter decade; in the white female population the rate increased 42 per cent. The rapid increase in the death rate from cancer of

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the respiratory system is in striking contrast ~~from cancer of~~ to the change in the death rate for all forms of cancer. During the decade 1930-1940 the death rate from all forms of cancer among white females actually decreased although the amount of the decrease was negligible (only ~~1~~ one per cent). The corresponding rate among white males increased about ~~10~~ ten per cent, but this increase was considerably less than the increase for respiratory cancer, including cancer of the lung.

Dorn (1943) stated that the [redacted]ed increase in the death rate from respiratory cancers is due primarily to an increase in late adult life. During the decade 1930-1940, increases in the death rate from cancer of the lung were confined to males of 35 or more years of age and to females 45 or more years of age. At the younger ages, the death rates in 1939-1940 were actually lower than the rates in 1930-1931. According to Dorn, cancer of the respiratory system develops more frequently among males than among females in contrast to all forms of cancer as a whole. On the average, the death rate from all forms of cancer was about 9 per cent higher for females than for males, but the rate for cancer of the lungs and pleura among males was nearly 2.5 times that among females and for all forms of ~~cancer~~ respiratory cancer the rate among males is more than ~~3~~ thrice times the rate among females.

Because no accurate records of the total number of living persons with malignant neoplasms were available, the United States Public Health Service in 1938 began to collect such records in a[illegible]

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~~number of~~ urban areas where it was believed that hospital and medical facilities were accessible to all groups of the population. According to the data collected through 1942, nearly 3 per cent of the 39,970 cases of cancer in the living white population were reported to have ~~a~~ primary cancer of the lung. This figure is only slightly less than the percentages of all deaths from cancer which is attributed to cancer of the lungs and pleura, namely, 3.5 per cent.

Dorn (1943) extrapolated his data ~~through~~ to the entire population of the United States and estimated that between 450,000 and 500,000 persons in the United States are under medical treatment for cancer each year. In addition, there are an unknown number of persons with undiagnosed cancer as well as those who have been treated for cancer and are now "cured". During the period 1938-1942 approximately 20,000 of the ~~new~~ cases of cancer under treatment each year had ~~have~~ a primary cancer of the respiratory system; of these about 13,000 were ~~are~~ being treated for primary cancer of the lung. Slightly more than 8,000 new cases of the primary cancer of the lung were ~~are~~ diagnosed and received medical treatment for the first time each year. Nearly ~~x~~ 5,000 additional cases with primary cancer of other parts of the respiratory system were ~~are~~ also diagnosed, making a total of approximately 13,000 new cases of primary cancer of the respiratory system that were given medical care for the first time each year.

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Steiner (1944) reported that in the period 1902 through 1941, primary bronchiogenic carcinoma was found in 126 out of 5,515 autopsies at the University of Chicago. The incidence of ~~primary~~ lung cancer was 2.3 percent of all autopsies ~~necropsies~~, 7.6 percent of all malignant tumors, and 10.3 percent of all ~~tumors diagnosed as~~ carcinomas, ~~xxxxx~~ The incidence of carcinoma of the lung expressed in percentage of all tumors showed a slight increase in males over the period, but not in females. This increase, however, was less than that shown for ~~xxx~~ carcinoma of the colon and for intracranial tumors, but greater than that for carcinoma of the pancreas and of the stomach. Steiner made corrections for changes in the annual number of autopsies, in the sex ratio, in the percentage of neoplasms in all autopsies, and in the average age of the autopsy population. ~~Steiner~~ He concluded that the only variable not subject to correction, the changing nature of patients admitted to the hospitals, could easily account for the slight increase in lung cancer observed. He believed that there has been a slight apparent, but no real, increase in primary bronchiogenic carcinoma.

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STUDIES OF LUNG CANCER INCIDENCE PUBLISHED DURING 1946 - 1947:

Some data on lung cancer incidence published during the period 1946-1947 have already been presented in tabular form in the preceding section of this chapter, and need not be restated here.

Clemmesen and Busk (1947a, 1947 b, 1947c) studied the mortality statistics for Denmark from official mortality records for the period 1931-1945. They concluded that in Denmark there has been an apparent rise in the incidence of lung cancer males, which since 1931 had increased from about 5 per 100,000 in Copenhagen to about 25 per 100,000 in 1945. These workers attributed a large part of this rise to better diagnosis, because the increase was smallest in country districts, somewhat greater in towns, and greatest in Copenhagen. These workers also analyzed material from the Central Tuberculosis Station at Copenhagen from 1936 to 1945 and reported only a slight increase in the incidence of lung cancer, but less pronounced and less constant than in the above series. Heady and Kennaway (1949) criticized the generalization of Clemmesen and Busk (1947) that the increased frequency of lung cancer was associated with better diagnosis, on the grounds that it was based on only a few cases each year drawn from a specialized population and that the mortality figures derived showed no steady trends

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Kennaway and Kennaway (1936, 1947) analyzed the death certificates for cancer of the lung and of the larynx in males from England and Wales for the period 1921-1938 inclusive (numbering 38,418), and compared in detail the periods 1921-1932 and 1933-1938. These workers recognized and examined the errors which are inherent in the use of death certificates for statistical purposes. Deaths from cancer of the lung in males increased from 361 in 1921 to 5,982 in 1945 with the trend in the intermediate years being almost linear. In contrast, deaths due to cancer of the larynx underwent no marked increase during the same period, remaining between about 600 and 800 deaths.

Stocks (1947), using data from the registration of deaths for England and Wales (standardized to allow for population changes) reported the following trend in lung cancer incidence: Rate per 100,000 in 1901-1920, males 1.1, females 0.7; rate per 100,000 in 1936-1939, males 10.6, females 2.5. According to this worker, the rise seemed to have been particularly rapid after the end of World War I, and between 1921-1930 and 1940-1944 the lung cancer death rate of men at ages 45 and over increased sixfold and of women of the same ages approximately threefold.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Denny (1947) reported that in Eire cancer of larynx, trachea, lung and mediastinum manifested a marked rise in mortality incidence during the period 1935-1945. This was especially true of lung cancer, and Denny concluded that this finding was due to the increased use of radiography. In 1936, 124 cases of lung cancer were recorded, and 209 cases in 1945.

Potter reported in 1947 that during the previous twelve years the adjusted mortality rates for cancer of the stomach, buccal cavity, skin, uterus and liver showed downward trends for the white population of the continental United States. The rates for cancer of other sites, including pancreas, testes, prostate, intestines, lung and "other respiratory" sites, showed upward trends. Cancer of the larynx (female), vulva-vagina, breast, scrotum, bladder, esophagus, kidney (female), and rectum (female) showed no significant trend.

[redacted]

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STUDIES OF LUNG CANCER INCIDENCE PUBLISHED DURING 1948-1949:

Some data on lung cancer incidence published during the period 1948-1949 have been presented in tabular form in an earlier section of this chapter and need not be restated here.

Churchhill (1948) stated that nothing is known about the causes of primary carcinoma of the lung that can be translated into effective preventive measures. He held it possible that an actual increase in the incidence of pulmonary cancer has taken place during the first half of the century.

O'Keefe (1948) analyzed 131 cases of primary lung cancer and attempted to correlate the data with recent literature. He concluded that statistics support the view that the incidence of this disease is increasing both absolutely and relatively.

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Simonds (1949) reported a study of 98 cases of primary carcinoma of the lung encountered among 4,590 autopsies done in during the period 1929-1948 in six general hospitals in Chicago. The entire 98 cases were used for certain statistical studies and 83 cases for a more detailed analysis. In this series, bronchogenic carcinoma increased from 1.18% of all autopsies between 1929 and 1933 to 3.22% between 1944 and 1948, while carcinoma of the stomach increased from 2.25% to 3.5% during the same periods. Simonds also discussed data based on 1,146 autopsies (included in the above series of 4,590 autopsies) performed at Alexian Brothers Hospital in Chicago. This institution accepts only male patients, many of them elderly men. In this hospital, primary carcinoma of the lung increased from only 0.47% of all autopsies between 1929 and 1933 to 4.95% between 1944 and 1948, while carcinoma of the stomach ranged from 6.07% to 4.37% during the same periods. Simonds called attention to how tricky statistics can be, for it was not until 1939, that this hospital acquired a chest surgeon!

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Springett (1949) compared Norwegian data on cancer of the respiratory tract with the incidence in England and Wales. In 1946 [redacted] mortality from cancer of the larynx in Norway was only one-fourth that in England and Wales. This geographic difference was still greater with regard to [redacted] deaths from cancer of the lungs, the mortality being five times higher in England and Wales than in Norway. During the past 25 years, there was little change in the ratio of [redacted] deaths from cancer of the larynx to [redacted] deaths from all forms of cancer in either country. In both countries and in both sexes there has been a rise in [redacted] mortality from cancer of the lungs, which in the case of women in England and Wales rose from about one percent to three percent of all cancer deaths during the last 25 years. Springett concluded that the low mortality from cancer of the larynx and lungs in Norway, as compared with that in England and Wales, cannot be explained by references to differences in the registration and classification of these diseases in the [redacted] two countries. He assumed that other unknown factors are operative. Springett stressed [redacted] that, while the relative mortality from cancer of the larynx has shown no great change in either Norway or England during the last 25 years, the relative mortality from cancer of the lungs has shown a decided rise in the same period in both countries [redacted] ales in England and [redacted] ales).

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Fulton (1949) surveyed the incidence of lung cancer in the cancer registration program of the Liverpool Cancer Control Organization in the five-year period 1944-1948. In 1944, 210 cases of lung cancer were reported, and in 1948, 456 cases [illegible]. This increase, according to Fulton, was probably due to better cooperation by [illegible] hospitals. The incidence of primary lung cancer in the Liverpool area per million population in 1944 was 145 and in 1948, 207.

Adams (1949) observed that cancer of the lung accounts for about seven percent of all cancers.

Mason (1949) recorded that the lung cancer mortality in England and Wales for 1902-1910 was 10.2 per million (standardized) for males and 7.0 for females. For 1937, the corresponding figures were 100.9 and 23.2. This worker felt that it was impossible to decide whether this increase was real or apparent. He held that during recent years even though much had been made of such figures as suggesting a real increase, it must be remembered that cancer of the lung has increased in clinical interest, improved diagnosis and treatment has come into being, and a greater proportion of patients die in hospitals with active pathology departments rather than [illegible] homes or in sanatoria.

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STUDIES OF LUNG CANCER INCIDENCE PUBLISHED DURING 1950 ~~1952~~:

Some data on lung cancer incidence published during 1950 have been presented in tabular form in an earlier section of this chapter and need not be restated here.

E. M. Brockbank (1950) observed that there has been in England and Wales a steady and progressive increase in deaths due to ~~lung~~ cancer of the respiratory system, and cited the following data taken from the registration of deaths:

CANCER OF RESPIRATORY SYSTEM, REGISTERED MORTALITY, ENGLAND AND WALES (BROCKBANK, 1950)

Year	Males	Females
1937	4089	1162
1942	5596	1525
1943	6094	1581
1947	8063	2019

Ariel and co-workers (1950) reported a study of 1,205 cases of primary lung cancer. They concluded that an absolute increase in the incidence had transferred this condition from a position of an infrequent clinical entity to one of the most common of all neoplastic processes. For the period 1931-1946, 6.9 percent of all neoplasms seen were lung carcinomas, that is, of 17,327 neoplasms, 1,205 were lung cancers. They reported that the [redacted] incidence of lung cancer compared

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to all neoplasms showed a gradual increase from 2.1 percent in 1931 to 11.7 percent in 1946. No significant rise in gastric cancer incidence was observed during the same period. Laryngeal cancer cases increased (2.2 percent in 1932, 5.1 percent in 1946), but bladder cancer remained almost stationary. Ariel and co-workers concluded that lung cancer was the only type that had shown a relatively important absolute increase in yearly incidence.

Doll and Hill (1950) observed that according to the registration of deaths for England and Wales, the annual number of deaths attributed to cancer of the lungs increased from 612 in 1922 to 9,287 in 1947, or about fifteenfold during that quarter century. This large increase was held to be out of all proportion to the increase of population, either total or by age groups.

According to Spencer (1950), the American Cancer Society, studying nation-wide figures for 1946 found that in the male population the reported rate of lung cancer deaths has doubled in the past fifteen years and is now more than five times as high as it was 35 years ago.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Insert 9 → In an earlier study using necropsies at the University of Chicago from 1901 to 1943, Steiner (1944) concluded that carcinoma of the lung had increased only slightly more than cancer in general or than a number of other types of cancer, including cancer of the colon and intracranial tumors. Later, Steiner and co-workers (1950 b) were surprised to find by similar methods of analysis of the Los Angeles County Hospital necropsies (1918-1946), a great increase in lung cancer, disproportionate to that of cancer in general or to the same control types of tumor. They believed that these findings represent a real difference in the two materials, and possibly in the two communities.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

The Statistical Research Section of the American Cancer Society compiled a summary of the lung cancer deaths in the United States for the year 1947 based on Vital Statistics of the United States for that year (Watson, 1950). There were 14,666 deaths due to cancer of the lung and bronchus representing a death rate per 100,000 persons of 10.2. Of this number, 11,546 were in males and 3,120 in females. More than 12 percent of all male cancer deaths and 3 percent of all female cancers were due to cancer of the lung and bronchus in 1947, or 7.7 percent of all cancer deaths in that year.

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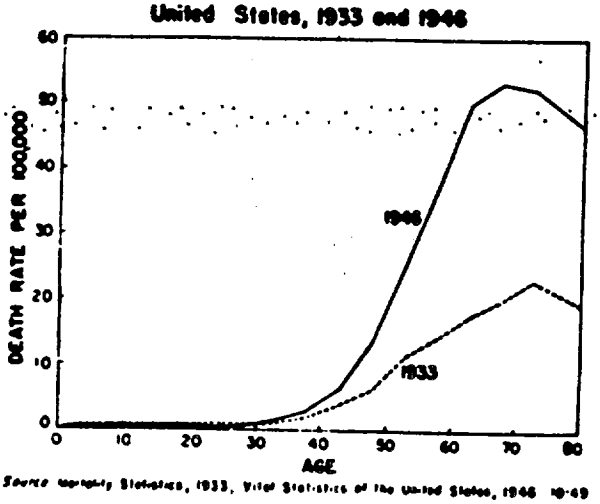
Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Watson (1950) compiled from the United States mortality statistics for 1933 and the Vital Statistics of the United States for 1946 a graph showing the respiratory cancer death rate for both males and females by age. His graph is reproduced below:

RESPIRATORY SYSTEM CANCER DEATH RATES BY AGE

United States, 1933 and 1946



Source: Mortality Statistics, 1933, Vital Statistics of the United States, 1946 pp 49

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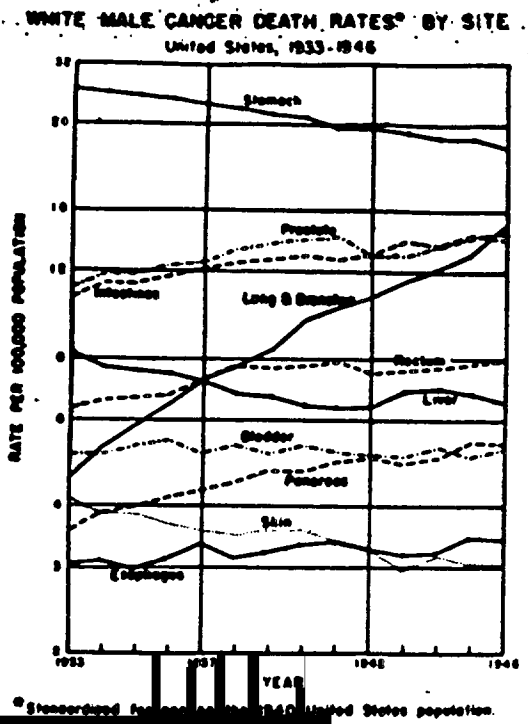
Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Watson (1950) presented ~~graphical~~ data graphically showing the death rate of cancer of various sites for the period 1933 to 1946, the data being standardized for age on the 1940 United States population. The graphs of Watson are reproduced below:



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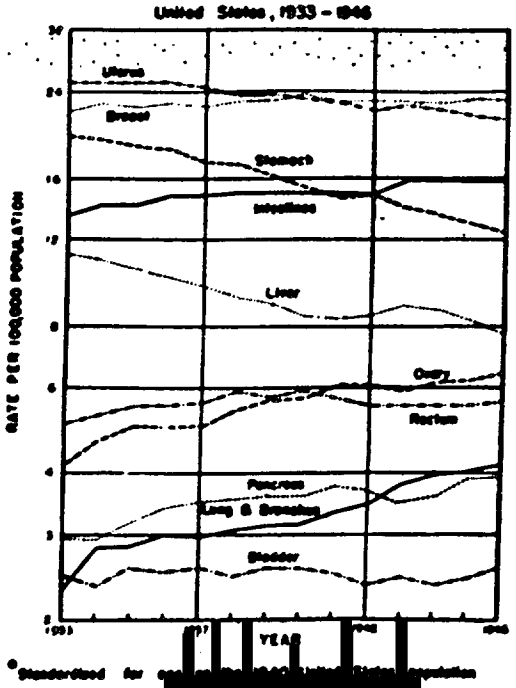
Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

WHITE FEMALE CANCER DEATH RATES* BY SITE

United States, 1933 - 1946



*Standardized for

Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

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Watson (1950) concluded from the above graphs that from 1933 to 1946 the incidence of cancer of the lung in males has shown a sharp increase in rate without a corresponding increase in the number of cancers of the stomach, prostate, bladder, skin, esophagus, etc. Further, cancer of the lung in females has increased in relation to malignant disease of the ovaries, breast, uterus, and stomach.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Huismann (1943) discussed at length a statistical study made by Vaandrager of Dutch mortality statistics for 1931-1939 with special reference to deaths due to pulmonary tumors in persons over 25 years of age. To make statistical reasoning more valid, the actual number of lung cancer cases in males and females observed in each year were adjusted to the ratio observed in 1936, and the adjusted figures calculated reduced to the basis of lung cancer mortality per 100,000 persons. On this basis, the mortality in Holland from lung neoplasms per 100,000 persons increased from 10.25 in 1931 to 21.63 in 1938 for males, and from 3.55 to 4.51 respectively for females. Application of tests for statistical significance suggested that the increased incidence rates were not chance occurrences.

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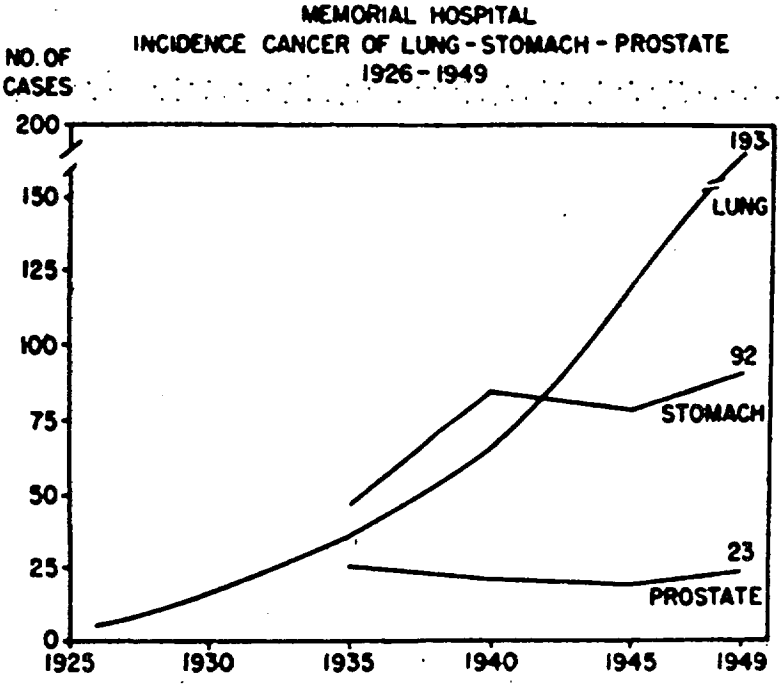
Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Watson (1950) presented data on the incidence of cancer of the lung, stomach and prostate at Memorial Hospital, New York through 1949. His graph is reproduced below:



In analyzing this graph, Watson stated:

> "From 1926 to 1933, a very small number of lung cancer patients were seen ~~at~~ Memorial Hospital, but from 1935 to 1940 there was a sharp rise in the incidence, and shortly after 1940 the admissions for cancer of the lung crossed the line for cancer of the stomach and went on to a precipitous rise in 1945, and continued through 1949, when a total of 193 patients with cancer of the lung were seen at Memorial Hospital. It may be of significance that the increase started ~~in~~ 1935 ~~was~~ more or less coincidental with Dr. Graham's report of the first successful pneumonectomy for cancer of the lung, and the almost vertical rise from 1945 on coincides with the general introduction of the antibiotics, penicillin, streptomycin and aureomycin."

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

In an anonymous (1950) report, the following facts were set forth: Age-adjusted death rate from respiratory cancer rose almost 80% among white industrial policy holders of the Metropolitan Life Insurance Co. at ages 1 to 74 - from 5.6/100,000 (1936-38), to 10.0/100,000 (1946-48). Mortality from all other forms of cancer as a group decreased somewhat. Both sexes showed an increase, but the death rate among white males is now almost 6 times that among white females, as compared to less than 4:1 a decade earlier. Among white males the death rate rose in every age group, the rise increasing progressively with each advance in age. Among the white females the rise occurred mainly in age groups 45-74. Of interest is the following: - "It is very likely that the rise recorded for cancer of the respiratory system is spurious in part at least, and represents the detection of an increasing number of cases through improved diagnosis". It was also stated that for cancer of the larynx (i.e. a site directly accessible to diagnosis and treatment) the death rate remained the same. For the rest of the respiratory tract (i.e. not directly accessible) there was a sharp rise. Cancers of the lung and pleura in white males increased by 87% and of the bronchus and trachea by 24%.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Indent 9 → Bryson and Spencer (1951) presented a clinical and pathological survey of 866 fatal cases of bronchial carcinoma in all of which necropsy and histological examination had been made by the staff of the London County Central Histological Laboratory. Clinical notes were gathered from 26 hospitals (formerly under control of the London County Council) and situated in the Greater London area. During the period covered by the investigation (1936-1947 inclusive) the laboratory staff was almost unchanged and technique of necropsy remained unaltered. All hospitals involved were non-teaching institutions obliged to accept patients suffering from any non-infective illness, and many patients had been transferred from teaching hospitals. Thus Bryson and Spencer felt that the possibility of error due to selection of clinical material was slight. From their data they arrived at the following conclusions:

Quotation single spaced

"Although the period covered by the survey is relatively short, certain features of interest emerge from the data after analysis. In spite of the strong personal impression of the authors to the contrary, it was shown in comparing the triennia 1936-8 and 1945-7 that the incidence of carcinoma of the bronchus did not increase in relation to the other common sites of primary carcinoma. The proportion of bronchial carcinomata to all forms of malignant disease remained nearly constant. The reputed increase in the in-

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

cidence of these growths during the period under review would thus seem to be more apparent than real. The great preponderance of the disease in men was again confirmed, the proportion of male to female patients being almost six to one. Despite the greater longevity of women, the peak incidence of the disease in women was at a slightly later age than in men, a fact which was found to be of statistical significance. Occupational factors did not appear to be related to the occurrence of the disease, but, as stated above, the information available was very inadequate.

The high proportion of men who gave a long antecedent history of cough and chronic bronchitis may be of importance, for these symptoms may have been related to heavy smoking which has been thought by some to be a factor in the aetiology of carcinoma of the bronchus. Other previous diseases of the chest, including tuberculosis, were shown to be of no significance."

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Indent ¶ ——→Gsell (1951) analyzed 126 cases of bronchial carcinoma and corroborates four findings which have hitherto been reported from various other sources.

A. There has been a sharp increase of bronchial carcinoma within the last 30 years.

B. Bronchial carcinoma is a disease of the higher adult age groups. (It starts at the age of 30 and is most frequent in the 50-70 year range.)

C. Bronchial carcinoma is predominantly a male affliction, 88.9% of the present cases being male giving a ratio of 1:8.

D. Histologically, bronchial carcinoma shows a preponderance of epidermoid or squamous cell carcinoma and its variants, and of the undifferentiated carcinoma. They both comprised 91.8% of the present cases. The adenocarcinomas represent only 6% of the cases.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

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Student #—> In an editorial appearing in the Journal of the American Medical Association (1951), the following statement appeared. -

"Numerous surveys have indicated that the incidence of carcinoma of the lung has been increasing in recent years. There is no general agreement, however, as to whether this increase is real and absolute or merely apparent and relative owing to such factors as better diagnosis, increasing clinical awareness of the condition, and the increase in life expectancy."

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Insert A --> The study of Fruhling and Horrenberger (1952) was based on the following material obtained at the Institute of Pathological Anatomy in Strasbourg:

1926 thru 1930	-	total autopsies	4,573
1946 thru 1951	-	total autopsies	3,608
1926 thru 1930	-	Adult autopsies (i.e. over 20 years)	2,966
1946 thru 1950	-	Adult autopsies (i.e. over 20 years)	2,152

When evaluating their results they considered the following factors:

1) The relatively limited number of autopsies used for their study (as compared to material of other authors). They argued, however, that the general population included in the autopsy data was in no way selected and therefore, perfectly usable. In addition, whether analyzing the results by 5 year periods or year by year, the increase was homogeneous.

2) The factor of professional differentiation by the pathologist. The authors stated that their two series were in this respect as homogeneous as possible, since all autopsies were made by pathologists by profession, who shared the same views on the problem of lung cancer diagnosis at autopsy.

3) As regards the possible factor of improvements in autopsy of lung cancer, they state that there has been no appreciable progress

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

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in this particular field for the past 50 years.

4) Similarly, one could say there was an element of variation conditioned by improvement of clinical diagnosis. It would be logical to presuppose that having diagnosed lung cancer more often, the clinicians would also have required autopsy verifications more often than a few years previously. From the two series in this study, "it is evident that as regards the group of lung cancers autopsied, clinical diagnosis has made no appreciable progress (as corroborated by Becker at the Pathological Institute of Giessen)."..."This factor has not varied during these last two decades, nor has the group of lung cancer autopsies been more selective from the clinical point of view," ~~since twenty years ago~~.

Quotation single spaced

5) ~~Concerning the~~ Variation in the percentage of autopsies in relation to general mortality figures, ~~this~~ was definitely a factor. During the period 1926-30, 78.34% of the patients who had died were autopsied, whereas in 1946-50, this figure dropped to 51.22%. This low percentage of autopsies versus general mortality, far from increasing the number of pulmonary cancer cases diagnosed at autopsy, definitely decreased it. The increase in lung cancer mortality is indeed a real one, and the coefficient obtained in this study expressed a minimum value for the given population.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

6) As for the sex factor, though the proportion of male autopsies to female has been absolutely constant for the two decades, the incidence of lung cancer is definitely greater in the male.

7) "Hospitalization from the social point of view ~~is of course~~ has resulted from recent social laws which have been instituted in certain countries. In the eastern provinces of France the question is a bit different: a medico-social organization very similar to the present-day Social Security was actually introduced in 1919." The authors feel well justified in stating that in their statistics the quality of hospitalization has remained the same since 1926. Though there has been a consistent increase in the number of patients hospitalized in the City Hospitals of Strasbourg (comparing periods 1926-30 and 1936-50) the mortality rates have remained perfectly constant, which in the opinion of the authors, indicates the homogeneity of hospital admissions.

8) The increase in average age of the general population at autopsy explains the slight increase in a number of cancers (e.g. gastric, esophageal, hepatobiliary, cerebrospinal) but not the great increase in lung cancer incidence.

"The profound causes of this increase are not apparent."

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Rigdon and Kirchoff (1952) wrote a review in which they made some interesting interpretations of earlier reports which are deemed worth repeating here. The authors said: "There is such a wide variation in the significance of the theories advanced to account for the increase in the frequency of cancer of the lung that the data, in our opinion, do not justify the conclusion that cancer of the lung has actually increased as a result of any one so far advanced. The statistical data presented by some investigators relative to cigarette smoking are impressive; however, there is such a wide variation in control samples that, in our opinion, additional sampling is needed to warrant their conclusions. There is no significant correlation between the amount of tobacco consumed and the death rate for cancer of the lung in the United States. There is, however, a significant correlation in the United States between the population to physician ratio and the population to bed ratio and the number of reported deaths from cancer of the lung. Better diagnoses, decrease in the number of deaths from infectious diseases by both prevention and therapy, and the increase aging of the population seem to be more significant factors than any one or group of carcinogens to account for the apparent increase in the frequency of carcinoma of the lung."

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Indent 9 — Hammond ~~Cuyler~~ (1952) states as follows:

"The increase in cancer of the lung has occurred in all sections of this country and in most other countries from which we have reliable statistics. Therefore, it may be assumed that it is due to some factor or factors operating over very wide areas and in very different types of communities. Furthermore, it would seem to be a reasonable hypothesis that there has been a corresponding increase in one or more of the major factors, at present unknown, which are responsible for lung cancer. If it is discovered that lung cancer is indeed caused by some carcinogenic substance or substances of widespread and increasing use in our civilization, there is reason to hope that we may be able to control the disease by eliminating the cause."

Quotation single spaced

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

THE INCIDENCE OF VARIOUS CANCERS:

Barron (1922) reported that carcinoma of the lungs and bronchi ranked sixth among all malignancies. Rosahn (1930) placed it fifth. Rosedale and McKay (1936) in a series of 466 malignancies of all types reported that carcinoma of the lung was the third most common cancer. Arkin and Wagner (1936) ranked this condition second in frequency only to malignancies of the gastro-intestinal tract. Brines and Kenning (1937) found the lung second to the stomach as a site of primary neoplasms in their autopsy material and fifth among their surgical specimens. Klotz (1938) and Boyd (1939) reported that during the 10-year period ending in 1936 in autopsies at the University of Toronto, the lung and bronchi were the third most common site for malignant tumors, being preceded in frequency only by those of the stomach and large bowel. Roffo (1939d) stated that in a series of 78,000 patients (presumably all with cancer) cancer of the smoking tract ranked first in incidence. Rosahn (1940) reported that of all carcinomas autopsied at the Yale University School of Medicine in the decade 1917-1927, primary pulmonary tumors ~~was~~ were fifth in frequency, while in the following decade ~~it~~ they rose to second place, being exceeded in incidence only by malignancies of the large bowel.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Indent ¶ → Henschen (1947) found in a combined series of 10,000 cancer autopsies that lung cancer was second in incidence with intestinal cancer, gastric cancer being in first place.

Indent ¶ → Koch (1950) reported that in autopsies at the Düsseldorf Pathological Institute since 1942 cancer of the lung has been the most common male cancer with that of the stomach second. Emminger and Einfalt (1950) reported that in autopsies at eight Bavarian pathological instituted during the period 1945-1948 gastric cancer was the most frequent malignancy (25 percent) in males over twenty years of age with bronchiogenic carcinoma a close second (21.4 percent).

[redacted]

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

According to Spencer (1950), the American Cancer Society, studying nation-wide figures for 1946, stated that among the 88,801 men who died that year from cancer, the malignancy was in the stomach in 15,984; in the prostate in 10,616; in the intestine in 9,929; in the lung or bronchus in 9,877. Pulmonary cancer, with an annual mortality of 14 per 100,000 of the male population was practically even with intestinal cancer - 14.1 deaths per 100,000 males - the foremost malignancy in men, and was not far from second place. According to Spencer, pulmonary cancer almost equaled as a cause of death the combined totals of the next two on the list: cancer of the rectum and cancer of the liver and bile passages.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Steiner and co-workers (1950_b) found that in necropsies performed from 1918 to 1949 at the Los Angeles County Hospital, carcinoma of the lung ranked fourth among malignant tumors, and in one recent 4-year period (1943-46), it was first.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Jost (1951) said: "In recent years a sharp increase in lung cancer incidence has been observed all over the world. Dormann's statistics for 1925-33 show that lung cancer mortality in males occupy fourth place and in females seventh place. The data of Einhalt for 1945-47 reveal that today lung cancer in males has risen to second place, while in females there has been no substantial rise. The number of cases in the very young age group has been extremely small."

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Anonymously (1951), the following observations are of interest. The postwar cancer record of the Metropolitan Life Insurance Co. industrial policy holders for periods 1946-47 and 1949-50 showed reductions in mortality among white females at ages 25-74 years, and only slight changes at ages 1-24 years. Among white males there was a decrease at ages 1-14 years and only a small increase at ages 15-24 years. However, ages 25-44 years showed a 12.6% increase and ages 45-74 years about 3.5%. For the accessible sites both sexes showed a decline, the white males by 2.4%, the white females by 7.2%. Among the latter, for each accessible site listed (except the breast) the mortality trend was downward. (The breast: no change). Among the males the only important site to show a decline was the buccal cavity and tonsils (13%). For the inaccessible sites, the females had a 1.1% decrease; the males a 4% rise. Both sexes showed decreases for such sites as the stomach, the intestines and duodenum, the rectum and anus, the liver and biliary passages, a residual category consisting of other digestive organs and the peritoneum, and the bladder. However, several inaccessible sites showed sizable increases: the lung, pleura, mediastinum, bronchus, and other respiratory parts, and the pharynx. Taken together, these sites showed an increase of

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30.4% in white males from 1946-47 to 1949-50, and by 10.3% for white females. The factors considered important were: improved diagnostic techniques, increasing alertness of the physician, and to some extent, cancer detection incidental to mass X-ray examinations.

The conclusion was: "However, it is not yet apparent to what extent these and other unknown factors are contributing to the marked upward trend in these cancers."

~~Both sexes also had a rise in mortality from cancer of the pancreas.~~

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

9 Fruhling and Horrenberger (1952) observed that the relative increase of lung cancer, having changed from 5.10% to 18.7% of all cancers, had risen within 20 years by 3.7 times and when arranged among all cancers in their order of frequency pulmonary cancer had jumped from seventh to first place.

As regards absolute increase of lung cancer, for these figures the authors used death rates and purposely did not differentiate between: "died of lung cancer" and "died with lung cancer." Thus, lung cancer deaths (for the same twenty-year period) increased from 0.84% to 4% that is 4.75 times, whereas cancers of other sites have shown little variation. Furthermore, they state, the increase has not been the same in both sexes, but more prevalent in the male.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

By means of two graphs, Hammond (1952) shows that the standardized death rates from cancer of the stomach and cancer of the liver have been steadily declining, particularly among males. On the other hand, cancer of several sites (e.g. pancreas) have increased somewhat, though not much. Cancer death rates of most of the remaining sites remained practically the same. The one exception is the lung-bronchus category which has shown a steady and tremendous increase in age-corrected death rates (1933-1950).

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Indent A ----> Hewett and Brooksbank (1952) ~~at~~ of Oxford, England based their comparative study of cancer mortality in England and the United States on the following official sources:

Indent B

The Registrar-General's "Statistical Review of England and Wales"
"Vital Statistics of the United States"
"Causes of Death in the Kingdom of Denmark".

Their data cover the period 1946-1948 and the standard population adopted was that recommended by the International Statistical Institute from which a standard million of persons aged 35 and over was obtained.

TABLE 3

S.D.R.'s Per Million Living from Cancer of "Accessible" and of "Inaccessible" Sites: 1946–1948

Group	Accessible				Inaccessible			
	Males		Females		Males		Females	
	Rate	Per cent of E. & W.	Rate	Per cent of E. & W.	Rate	Per cent of E. & W.	Rate	Per cent of E. & W.
England and Wales	676	100	860	100	2,752	100	1,867	100
U. S. whites	617	91	797	93	2,081	76	1,874	100
U. S. nonwhites	419	62	641	75	1,929	70	2,054	110

In the above table they compared death rates from cancers of "accessible" and "inaccessible" sites and found that while female mortality from cancers of accessible sites shows the same order as that observed in the male ~~S.R.D.'s~~ S.D.R.'s, the rates for inacessible sites are in reverse order. Furthermore, as the percentage figures show, the dispersion of the rates is much greater for accessible

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

than for inacessible sites. Better chance of treatment cannot account for the variation observed, because the lowest of the three male rates for accessible sites is that for U.S. non-whites.

"It is more likely that the accessible sites in Table 3 include a high proportion of the sites most exposed to environmental influences and for this latter reason are more liable to be differentiated as between one country and another."

TABLE 6

Comparison of Standardized Death Rates (Per Million Living Over the Age of 35) for Cancer of Various Sites Among Males in England and Wales and in the United States: 1946–1948

Site	*England & Wales* Rate per million	*U. S. Whites* Rate per million	*U. S. Nonwhites* Rate per million	*U. S. Whites* Per cent of England and Wales	*U. S. Nonwhites* Per cent of England and Wales
Stomach	742	513	625	69	84
Lung and pleura	723	231	151	32	21
Intestine	439	344	223	78	51
Rectum	353	194	118	55	33
Prostate	245	351	391	143	160
Urinary	177	193	121	109	68
Esophagus	137	84	133	61	97
Pancreas	130	142	106	109	82
Liver	103	149	145	145	141
"Other" buccal cavity	93	90	67	97	72
Larynx and trachea	78	183	141	235	181
Tongue	55	35	28	64	51
Skin	49	69	22	141	45
Brain and C.N.S.	44	55	20	125	45
"Other" genital	28	21	30	75	107
Lip	14	18	4	129	29
Mesentery and peritoneum	12	19	14	158	117
Breast	6	7	9	117	150
Other unspec.	123	215	208	175	169
All Sites *	3,551	2,913	2,556	82	72
All Sites †	3,594	2,937	2,578	82	72

* Including respiratory system subtotals based on 1946–1947 only.
† Including respiratory system based on whole three years, 1946–1948.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

TABLE 7

Comparison of Standardized Death Rates (Per Million Living Over the Age of 35) for Cancer of Various Sites Among Females in England and Wales and in the United States: 1946-1948

Site	England & Wales Rate per million	U. S. Whites Rate per million	U. S. Nonwhites Rate per million	U. S. Whites Per cent of England and Wales	U. S. Nonwhites Per cent of England and Wales
Breast	597	551	446	94	74
Stomach	437	292	344	67	79
Intestine	414	390	241	94	58
"Other" genital	202	181	112	90	55
"Other" uterine	187	268	524	143	280
Rectum	178	138	122	76	69
Cervix	146	216	429	148	294
Lung and pleura	124	75	56	60	45
Liver	98	183	138	187	141
Pancreas	88	98	75	111	85
Urinary	71	95	83	134	117
Esophagus	58	22	28	38	48
Skin	29	41	19	141	66
"Other" buccal cavity	25	23	28	92	112
Brain and C.N.S.	25	34	12	136	48
Larynx and trachea	21	26	23	124	110
Mesentery and peritoneum	17	20	12	118	71
Tongue	9	8	8	89	89
Lips	1	2	1	—	—
Other unspec.	99	193	197	195	199
All Sites *	2,826	2,864	2,892	101	102
All Sites †	2,832	2,872	2,898	101	102

* Including respiratory system subtotals based on 1946-1947 only.
† Including respiratory system based on whole three years, 1946-1948.

In Tables 6 and 7 (above) the authors show how the S.D.R.'s for cancer of the various sites stand in order of importance. - In England and Wales the second place is taken by cancer of the lung and pleura, which is approximately three times the rate for white Americans and five times the rate for non-white Americans. On the other hand, the American S.D.R.'s for cancer of the larynx and trachea are substantially higher than the English rate.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

The mean age at death by site is also estimated and compared for the two countries. "When the various sites are considered in order of the relative age at death, cancer of the respiratory system is again found to show international contrasts. Mortality from cancer of the lung and pleura, which is much higher in England, is also associated with an appreciably earlier Standardized Mean Age at Death in England. With cancer of the larynx and trachea the position is reversed, American mortality being higher and occurring at an earlier age than in England and Wales."

By analyzing cancer mortality and economic status the authors find: "Some - but only some - of the differences between cancer mortality of the upper and lower social classes in England and Wales can be matched by corresponding differences between the white and non-white populations of the United States."

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DISCUSSION OF INCIDENCE STUDIES OF LUNG CANCER:

Indent A → That an increase in lung cancer has been recorded in most statistical series seems not open to question. However, underlying any such statement are the limitations of the very methods by which "increase" in a disease is measured. These methods, together with their limitations and inadequacies, have been discussed at length in an earlier section of this chapter entitled "Methods of Measuring 'Increase' in a Disease", and require little additional direct comment at this point.

Indent A → The question to be faced in a study of lung cancer incidence is not whether lung cancer is increasing in hospital incidence, but in the general population. There is no doubt that lung cancer is being diagnosed either clinically or at autopsy in hospitals more frequently today than it was in earlier years. But whether this increase is a real one or merely apparent when applied to the general population remains in doubt. Many of the shorter series of incidence figures based on data collected at only one or two hospitals are of little significance because the portion of the population coming to autopsy is so small and is not usually representative of the population (that is, social stratum is often reflected). Data from a single hospital must also be suspect as reduction in the number of diagnostic errors, improvement in diagnostic facilities and methods, introduction of new services and wards, and shifts in the nature and age distribution of the autopsy material would clearly affect the observed incidence trend markedly

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Fried (1948), after a brief review of literature, concluded that the incidence of bronchiogenic carcinoma is in "all likelihood more apparent than real". He suggested that the more frequent recognition of this condition today as compared with the past can be explained on the basis of the following factors:

"1. Progress in medicine in the past five decades resulting in improved methods of diagnosis.

"2. Progress in public health resulting in increased longevity (more people reached the 'cancer age'.

"3. A vastly developed means of hospitalization.

"4. Rises in the social and economic levels leading to more people seeking medical advice.

"5. Increased attention to the disease."

Some of these possible factors in the observed "increase" in lung cancer incidence are discussed in the following sections at some length.

LONGEVITY AS A FACTOR IN LUNG CANCER INCIDENCE:

Although increasing longevity (more people reaching the "cancer age") may be a factor to account for a portion of the recorded increases in lung cancer incidence in some statistical series, it must be recognized that this factor could not be the principal factor in such an increase. Even when ~~adjustments in~~ data are ~~made to~~ statistically standardized for changes in age distribution over a period of time - a procedure that minimizes the effect of longevity changes of the population - substantial increases in lung cancer have been observed in many studies (for example, those of Stocks, 1947; Huismann, 1943; Dorn, 1943). It must be recognized further that if

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

longevity were an important factor, it would be reflected not only in the lung cancer incidence/trend, but also in the trends for cancers of other sites. However, in many statistical studies of autopsy incidence, even when no correction was made for age distribution, no marked increase was observed in cancers of many sites in contrast to the huge increase in lung cancer recorded. ~~Hueper, Hiatt~~ Hruby and Sweany (1933) and many other workers have prepared graphs attempting to demonstrate a parallelism between increased longevity, increase in all forms of cancer, and an increase in cancer of the lung in particular. However, most recent workers (for example, see Klotz, 1938) have ~~stated~~ concluded that the increase in lung cancer is so much greater than the increase in all forms of cancer, ~~that the increase of cancer is so much greater than the increase in all forms of cancer,~~ that the increase in cancer of the lung cannot be explained on the basis of ~~increased~~ longer life expectancy.

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Steiner and co-workers (1950 b) do not believe that the disproportionate increase in lung cancer can be explained by the age factor for the following reasons. In the necropsy population studied by them, the death rate from cancer in each decennium was greatest in the decade 61 to 70 years (25.7%). Lung cancer had its peak a decade earlier, whereas carcinomas of the large intestine and pancreas had theirs 10 years later than lung cancer, and gastric cancer 20 years later. If the increase in lung cancer was due solely to aging of the population, then all cancers and the control carcinomas of the large intestine, stomach and pancreas should have increased even more, and intracranial tumors (whose peak incidence was in the second decade) much less. "That they did not do so is evidence that the increase in lung cancer was not explainable on this basis" says Steiner.

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> Blumer (1951) in an editorial expressed the belief that the increase in lung cancer, as with other forms of cancer, is partially due to the increased number of people living into the cancer age.

Quotation single spaced

"However, its marked preponderance in males, whereas the expectation of life is longer in females, leads one to question whether this is the sole factor."

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Hammond (1952) illustrated population trends very well by means of the following graphs:

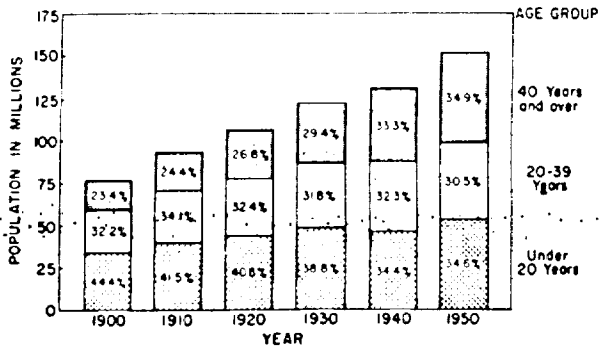

Chart 4.—Population trends in the United States from 1900 through 1950.

This shows that the total population of the United States had increased from 76 million (in 1900) to 151 million (in 1950) and that the age group 40-years-or-over had risen from 23.4% to 34.9% of the total population during the same 50 years.

Group	1933 Cancer Deaths	1948 Cancer Deaths	Increase 1933 to 1948	Change as Percentage of 1933 Cancer Deaths: Total Increase	Due to Population Changes	Due to Other Factors
White males	55,596	90,942	35,346	64	36	+ 28
White females ...	64,657	90,917	26,260	40	43	- 3
Nonwhite males...	2,990	7,002	4,012	134	32	+102
Nonwhite females.	5,236	8,181	2,945	56	44	+ 12
128	479	197	042	68	563	53	39	+ 13.7

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With the above data Hammond shows that there was an increase of 68,563 (53.4%) in the annual number of cancer deaths (1933-1948). Applying the 1933 age-specific cancer death rates to the 1948 population, he found that 51,064 (39.7%) more people would have died in 1948 than in 1933 owing to population changes alone. In other words, a 39.7% increase is due to the expansion and aging of the population during the 15-year period, which leaves an increase of 13.7% that must be due to other factors, like:

a) better diagnosis
b) increased "popularity" of cancer as a diagnosis when cause of death is uncertain.
c) perhaps an actual increase in cancer incidence.

At the same time, one other factor was operating to reduce the cancer deaths, namely, improvement in treatment and cure rates.

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THE EFFECTS OF IMPROVED DIAGNOSIS ON LUNG CANCER INCIDENCE:

In an early section of this chapter entitled "The Reliability of Cancer Statistics", many of the observations recorded in the literature concerning the frequent mis-diagnosis and non-diagnosis of lung cancer during life were summarized, and need not be restated here. It should be recognized that even in major hospitals where special facilities are available for the diagnosis and treatment of conditions of the lung, and where extensive X-Ray and broncho-scopic investigations are practised, the condition of bronchio-genic carcinoma is not infrequently mis-diagnosed.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Boyd (1939) pointed out that from the clinical standpoint there is no form of tumor which is more easily overlooked than that of the lung, especially if the case does not come to autopsy. Just as syphilis may mimic almost any other disease, according to Boyd, bronchiogenic carcinoma may masquerade as many other conditions. The clinician has only become familiar with these vagaries of lung cancer in recent years. Boyd felt that in the past there can be no question that large numbers of primary bronchial tumors were mistaken in the gross for Hodgkin's disease or for lymphosarcoma of the lung. According to this author, pathological museums are full of specimens of carcinoma of the lung which have been labeled as one of the lymphoblastomas. Another error, according to Boyd, is that tumor of the lung may be thought to be secondary in character, and one of the metastasis being mistaken for the primary condition. Increased understanding of the nature of the primary lung tumors in recent years has served to reduce this source of error. Boyd concluded that the fact that routine microscopic examination of autopsy material is much commoner today than formerly is one reason for the more frequent pathological diagnosis of bronchiogenic carcinoma.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Karshner in a discussion appended to the paper of Menne and Anderson (1941) observed that there can be no doubt of a relative increase in the incidence of bronchiogenic carcinoma, but there may well be some question as to an absolute increase. The population of the autopsy room may be different from the general population, because it is a population determined by numerous factors of opportunity and interest. In the ten-year period 1927 to 1937 inclusive, he reported, that at the Cleveland City Hospital bronchiogenic carcinoma constituted 9.4 percent of all cases of malignant tumor examined at autopsy. He felt that no one would claim that about one out of 10 living patients with malignant tumors has bronchiogenic carcinoma in spite of this data. Further, if autopsy statistics were a guide in this connection, it could be said that carcinoma of the lung arising in an obsolete primary tuberculous focus is on the increase, because this worker had seen three such instances in the last year as compared with none in the preceding 10 years. Karshner emphasized that it is difficult to employ statistical analyses in determining absolute increase, because there is no certain way to provide mathematical corrections that would fully account for improved diagnosis, special attention to the lesion, accurate interpretations of roentgenograms and precision of bronchoscopic examinations and biopsy.

According to Karshner, no formula has yet been devised that meets all the factors of error, largely because these factors are not yet calculable. An absolute increase according to this worker cannot be denied, nor is it fully established; the influence of various factors supposed to be responsible for an absolute increase is still in doubt.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Kennaway and Kennaway (1936, 1947) discussed whether or not errors in the diagnosis of cancer of the lung might account for the observed increase of cancer of the lung as the cause of death among males in England and Wales. They stated frankly that it was easy to claim that the ascent in lung cancers is due to improved diagnosis, and most difficult, perhaps impossible, to disprove. They pointed out that if one accepts such a view, then when the means of diagnosis and their availability can be improved no further, the yearly incidence curve for lung cancer must flatten. It cannot be said when this will happen, of course. These workers considered conditions which might give rise to false diagnosis in cases of cancer of the lung. These included mediastinal tumors, and pulmonary infections. It was observed, however, that there had been no fall in deaths attributed to cancer of the mediastinum, and in fact since 1931 the number of deaths due to this condition increased irregularly. The number of deaths attributed to respiratory tuberculosis and to pneumonia among all pulmonary infections are so large as compared with those ~~deaths~~ attributed to lung cancer, that any comparison of the two over a period of years in an attempt to demonstrate that the latter condition might have been misdiagnosed as a former condition to a greater extent in earlier years is clearly impossible. ~~The high percentage of erroneous diagnoses, as revealed at autopsy, has been noted by many workers.~~ Certain of these observations have already been discussed earlier in the section Cancer Statistics.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

E. L. Kennaway (1950) commented on the findings of Kennaway and Kennaway (1947) misquoted by others to suggest that they had reached the conclusion ~~held~~ that the increase in lung cancer in England was probably real, at least in part ~~to the effect~~, "The paper in question collects evidence from which the reader might form his own opinion, but this conclusion is not drawn".

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000

Stocks (1947), using data from the registration of death certificates in England and Wales standardized to allow for population changes, reported that between 1921-1930 and 1940-1944 the death rate of men at ages 45 and over due to lung cancer increased sixfold and of women of the same ages approximately threefold. Stocks believed that this increase in lung cancer incidence was a real increase, ~~ex~~ at least in part. He pointed out "The increase of certified respiratory cancer mortality during the past 20 years has been as rapid in country districts as in the cities of the best diagnostic facilities, a fact which does not support the view that such increase may reflect ~~the~~ some true diagnosis of cases previously certified as bronchitis or other respiratory infection". This worker also called attention to the differences in the mortality between some of the large cities in England and Wales, differences which are difficult to explain in terms of varied diagnostic standards.

Quotation single spaced

At the Toronto General Hospital, Gagnon (1948) reviewed 508 cases of bronchogenic carcinoma admitted to that hospital during the period 1934-45 and he believes the increase is apparent only, for the same reasons as advanced by Boyd (1939). Delarue (1952) continued this series through 1948 analyzing 124 cases, but states that the increase is a very real one.

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Source: https://www.industrydocuments.ucsf.edu/docs/rpbl0000